

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

Art Unit	: 1625	Customer No.:	035811
Examiner	: Taylor Victor Oh		
Serial No.:	: 10/542,498		
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Inventors:	: Seiji Morii	Docket No.:	TIP-05-1194
	: Toshihiro Fujino		
	: Haruyo Sato	Confirmation No.:	5310
Title:	: PROCESSES FOR THE RECOVERY		
	: OF OPTICALLY ACTIVE		
	: DIACYLTARTARIC ACIDS		

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**DECLARATION OF TOSHIHIRO FUJINO**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

I, Toshihiro Fujino, declare that I am an inventor named in the above-identified U.S. Patent Application and that I am thoroughly familiar with the above-referenced patent application and the subject matter described and claimed therein;

I and the other co-inventors disclose a process for recovering an optically active diacyltartaric acid from a salt of an amine and the optically active diacyltartaric acid in an acid aqueous solution in which an optically active diacyltartaric acid is added beforehand. I agree with the Examiner that both of JP '446 and JP '236 are silent with respect to the optically active diacyltartaric acid being added beforehand in the acid aqueous solution.

The reason for adding the optically active diacyltartaric acid in the acid aqueous solution beforehand is not to adjust the reaction condition (such as pH concentration, time, speed). The process is for industrially recovering an optically active diacyltartaric acid capable of being

easily used in recycling. More particularly, the process solves the problems of the prior art discussed from line 8 on page 6 to line 9 on page 7 in the Specification. When a salt of an optically active diacyltartaric acid is directly added into the stirred acid aqueous solution, the optically active diacyltartaric acid is precipitated, due to salt exchange, all at once to aggregate a block. Since the optically active diacyltartaric acid salt is also contained in the block, smooth salt exchange does not take place.

Comparative Example 1 in the Specification is an example that a salt of an optically active diacyltartaric acid is directly added into the stirred acid aqueous solution. In that case, "lumps stuck to the wall of the flask and did not form crystals," and "furthermore, the remaining diastereomer salt was added, taking about 2 hours, and the mixture was stirred overnight at room temperature. No crystalline di-p-toluoyl-D-tartaric acid was obtained." Such an optically active diacyltartaric acid will not be suitable for recycling.

On the contrary, Example 1 in the Specification shows, that the di-p-toluoyl-D-tartaric acid precipitated due to salt exchange was crystallized. Furthermore, the recovery rate is high (98%). Such an optically active diacyltartaric acid is suitable for recycling. The state of the recovered optically active diacyltartaric acid is good in slurry properties, and is also good in filtration properties (see lines 8 to 20 in the Specification on page 8). Furthermore, the recovery rate of the optically active diacyltartaric acid is high.

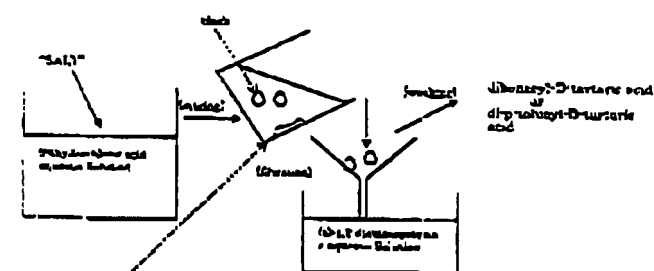
On the other hand, JP'446 and JP'236 only disclose the process that a salt of an optically active diacyltartaric acid is directly added into the stirred acid aqueous solution.

Neither discloses adding the optically active diacyltartaric acid beforehand in the acid aqueous solution, the state of slurry of the recovered optically active diacyltartaric acid, the quality of the recovered optical active diacyltartaric acid, nor recycling the recovered optical

active diacyltartaric acid. According to our studies, there are the above-mentioned problems in both of the methods of the prior art (see line 25 on page 1 to line 4 on page 2 in the Specification).

I enclose illustrations of the methods of the prior art and the claimed subject matter. The methods of Example 5 of JP '446 and Example 5 of JP '236 include:

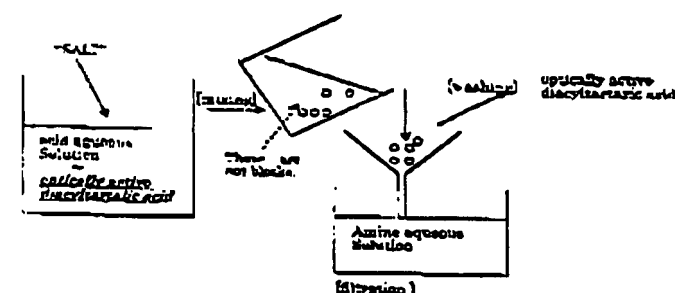
"SALT" is a salt of (S)-1,2-diaminopropane-dibenzoyl-D-tartaric acid in the case of JP '446, and is a salt of (S)-1,2-diaminopropane-di-p-toluoyl-D-tartaric acid in the case of JP '236.



"Lump stuck to the wall."  
It must be scraped together to recover it.  
If this were applied in a commercial process, recovery of lumps would be difficult.  
Even if lumps and blocks are recovered, they would not be suitable for recycling.

The claimed methods include:

"SALT" is a salt of an amine and an optically active diacyltartaric acid.



Both of JP '446 and JP '236 are therefore, inapplicable to all of Claims 1 - 7.

JP'446 is inapplicable to Claims 8-25 as well. First, JP'446 is the equivalent of JP

2712669 cited on page 1 of the Specification. The problems associated with JP'669/JP'446 have already established inasmuch as the diacyltartaric acid recovered by the solid-liquid separation of JP'669/446 is highly likely to be aggregated as a block, thereby necessitating a subsequent grinding step before recycling can occur. Also, when the aggregation occurs, it requires a long reaction time for the salt of an amine and an optically active diacyltartaric acid to be formed. Thus, the process disclosed in JP'669/446 is not practical for industrial use.

The following is a side-by-side comparison of JP '446, JP '236, Claim 1, Examples 1, 6 and 7 from our Specification,

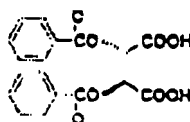
JP '446	JP '236	Claim 1	Example 1	Example 6	Example 7
			Racemic amine + DCT acid + Acid solution	Racemic amine + DCT acid + H <sub>2</sub> O	
↓ heat & cool, precip(optical resolution)					
Salt of amine + H <sub>2</sub> O			Salt of amine + H <sub>2</sub> O		
↓ heat & cool, precip(recrystallization)					
Salt of amine + Acid Solution	Salt of amine + Acid Solution	Salt of amine + Acid Solution + DCT acid	Salt of amine + Acid Solution + DCT acid	Salt of amine + Acid Solution + DCT acid	Salt of amine + Acid Solution + DCT acid
↓ precip					
DCT acid	DCT acid	DCT acid	DCT acid	DCT acid	DCT acid

## (1) Example 5 of JP '446



(S)-1,2-diaminopropane

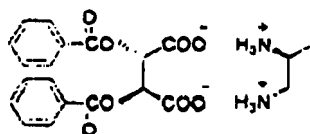
Amine: (S)-1,2-diaminopropane



dibenzoyl-D-tartaric acid

DCT acid: dibenzoyl-D-tartaric acid

Salt of amine : Salt of (S)-1,2-diaminopropane and dibenzoyl-D-tartaric acid = (S)-1,2-diaminopropane • dibenzoyl-D-tartaric acid



Salt of amine

## (2) Example 5 of JP '236

Amine : (S)-1,2-diaminopropane

DCT acid : di-p-toluoyl-D-tartaric acid

Salt of amine : Salt of (S)-1,2-diaminopropane and di-p-toluoyl-D-tartaric acid:  
= (S)-1,2-diaminopropane • di-p-toluoyl-D-tartaric acid

## (3) Claim 1 of the present invention

Amine : amine

DCT acid : optically active diacyltartaric acid

Salt of amine : Salt of an amine and the optically active diacyltartaric acid

## (4) Example 1 in the present specification

Racemic amine : 1,2-diaminopropane

DCT acid : di-p-toluoyl-D-tartaric acid

Salt of amine (Diastereomer salt) :

Salt of optically active 1,2-diaminopropane and di-p-toluoyl-D-tartaric acid

= Optically active 1,2-diaminopropane • di-p-toluoyl-D-tartaric acid

(5) Example 6 in the present specification

Racemic amine: 1,2-diaminopropane

DCT acid: dibenzoyl-L-tartaric acid

Salt of amine (Diastereomer salt) :

= Salt of optically active 1,2-diaminopropane and dibenzoyl-L-tartaric acid

= Optically active 1,2-diaminopropane • dibenzoyl-L-tartaric acid

(6) Example 7 in the present specification

DCT acid: dianisoyl-L-tartaric acid

Salt of amine :

Salt of optically active aminopentanenitrile and dianisoyl -L-tartaric acid

= Optically active aminopentanenitrile • dianisoyl -L-tartaric acid

JP'446 is different from the Applicants' Claim 8, for example. It should be noted that JP'446 discloses contacting a salt of an amino acid and a diacyltartaric acid with water, followed by heating and cooling to precipitate the salt of the amine and the acid. Then, an aqueous acid solution is added to the salt to precipitate the diacyltartaric acid. This is followed by the addition of a basic aqueous solution and distillation to isolate the amine.

This is sharply different from Claim 8, which does not start with a salt of the amine and the diacyltartaric acid. Instead, Claim 8 contacts amine, diacyltartaric acid and an aqueous acid solution. A diastereomer salt of the amine and the diacyltartaric acid is precipitated. Then, the diacyltartaric acid in an aqueous acid solution is added to precipitate the diacyltartaric acid. This is neither taught nor suggested by JP'446 and is not a reversal of the order of steps as suggested in the rejection. This is demonstrated in Exhibit A.

There are also differences between Claims 14 and 20 with respect to JP'446 as well. I enclose Exhibits B and C to illustrate that difference. Claim 14 does not begin by contacting a salt of an amine and a diacyltartaric acid plus water. Instead, it begins with the amine, the diacyltartaric acid and water. The solution of amine diacyltartaric acid and water is followed by a precipitation step which forms a salt of the amine and the diacyltartaric acid. This is followed by the addition of the diacyltartaric acid and an aqueous acid solution to precipitate the

diacyltartaric acid. In Claim 20, a salt of an amine and the optically active tartaric acid was added by dividing. A second addition of salt was after the dianisoyl-L-tartaric acid precipitated due to salt exchange was crystallized. Again, this is not a reversal of the steps.

The undersigned declares that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and thus such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: April 27, 2007

Toshihiro Fujino  
Toshihiro Fujino